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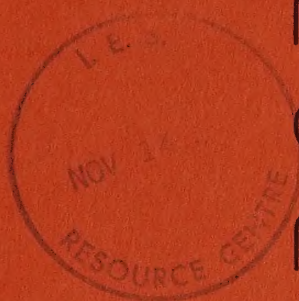
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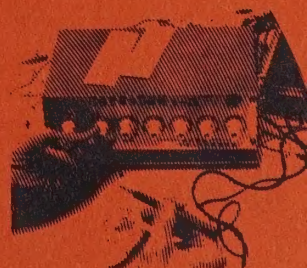
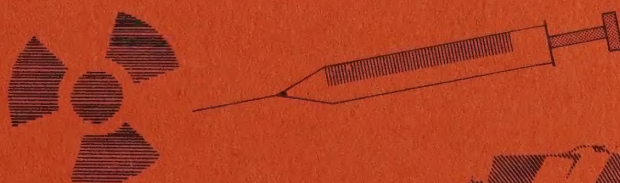
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nitrogen dioxide and nitric oxide/ recommendations for occupational exposure

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NITROGEN DIOXIDE AND NITRIC OXIDE
RECOMMENDATIONS FOR OCCUPATIONAL EXPOSURE

Environmental Health Directorate
Health Protection Branch

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FOREWORD

This report was prepared by staff of the Bureau of Chemical Hazards, Environmental Health Directorate in response to a request from Labour Canada for advice on occupational exposure to nitrogen dioxide. It has been made available as an Environmental Health Directorate publication in anticipation that such a document will prove useful to other government departments and labour groups responsible for safeguarding the health of workers.

In March 1976 the United States' National Institute for Occupational Safety and Health (NIOSH) published a criteria document entitled "Occupational Exposure to Oxides of Nitrogen, (Nitrogen Dioxide and Nitric Oxide)". Separate standards for nitrogen dioxide and nitric oxide were proposed and a recommendation made that the standard for occupational exposure to nitrogen dioxide be reduced from 5 ppm to a ceiling value of 1 ppm. In compiling the present report extensive use of the information presented in the NIOSH document has been made. Some of the more pertinent information covering sources of exposure, exposure levels and health effects has been summarized; the sections containing the descriptions of proposed analytical methodologies are attached as appendices to this report.

Other recent reviews, namely "Photochemical Air Pollution: Formation, Transport and Effects", (National Research Council of Canada, 1975) and "Environment and Quality of Life; A Preparatory Study for Establishing Criteria (Dose/Effect Relationships) for Nitrogen Oxides", (Commission of the European Communities, 1976) provide an overview of the problems associated with oxides of nitrogen in the general environment. Additional pertinent data presented in these reviews have been included and considered in arriving at the recommendations made concerning exposure to nitric oxide and nitrogen dioxide in the more specific situation of the workplace environment.

Acknowledgement is given to Dr. V.C. Armstrong, Environmental Standards Division and Dr. A. Sundaram, Environmental Toxicology Division, who were primarily responsible for the preparation of this report.

SUMMARY

Occupational exposure to nitrogen dioxide and nitric oxide may occur wherever there is a high temperature operation or a chemical process employing nitric acid, nitrates or nitrites. In many situations it is unlikely that one of these oxides will be present in the absence of the other. In order therefore to effectively control worker exposure to nitrogen oxides it is recommended that separate standards be adopted for nitrogen dioxide and nitric oxide. Smoking adds significantly to an individual's exposure to oxides of nitrogen. The possibility of exposure to nitrosamines, which may be formed from nitrogen oxides and secondary amines, is considered.

Both nitrogen dioxide and nitric oxide are highly aggressive and react immediately on contact with the respiratory tract. At low concentrations nitrogen dioxide is more toxic. Short-term exposure results in an increase in airway resistance, a reduction in effective lung compliance, a significant decrease in arterial oxygen tension and a decrease in carbon monoxide diffusing capacity. The toxic effects of exposure to low levels of nitric oxide are not well understood; data are still lacking to describe accurately the levels at which this pollutant presents a hazard to health.

A sampling device containing a solid adsorbent and proprietary solid oxidant provides a convenient method for monitoring simultaneously nitrogen dioxide and nitric oxide in the workplace; determinations may subsequently be conducted using a colorimetric procedure.

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A sampling device containing a solid absorbant and proprietary solid oxidant provides a convenient method for monitoring simultaneously nitrogen dioxide and nitric oxide in the workplace; determinations may subsequently be conducted using a colorimetric procedure.

III. RECOMMENDATIONS

1. Workers should not be exposed to nitrogen dioxide levels greater than a ceiling concentration of 1 ppm by volume (1.8 mg m^{-3}), as determined by a sampling time of 15 minutes.
2. In the absence of data clearly defining levels at which nitric oxide becomes deleterious to health it is recommended that exposure to this substance should not occur at a concentration greater than 25 ppm by volume (30 mg m^{-3}), determined as a time weighted average exposure for up to 10 hours per day and 40 hours per week.
3. Animal experiments have demonstrated a definite synergistic effect when exposure to nitrogen dioxide occurs in the presence of tobacco smoke. Workers should therefore be discouraged from smoking when the presence of nitrogen dioxide is suspected.



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I. INTRODUCTION

Eight different oxides of nitrogen have been identified; nitrous oxide (N_2O), nitric oxide (NO) and its dimer (N_2O_2), dinitrogen trioxide (N_2O_3), nitrogen dioxide (NO_2) and its dimer, dinitrogen tetroxide (N_2O_4), dinitrogen pentoxide (N_2O_5) and nitrogen trioxide (NO_3). Nitric oxide and nitrogen dioxide are commonly referred to collectively as NO_x and are the only two oxides of nitrogen of significance from the point of view of air pollution. They are formed at high temperatures as combustion products, by fixation of atmospheric nitrogen and by bacterial action on decaying proteinaceous material. Generally, nitric oxide is produced first and then oxidized to nitrogen dioxide; the photochemical conversion of nitric oxide to nitrogen dioxide occurs in the atmosphere via a complex sequence of reactions initiated by the dissociation of nitrogen dioxide to nitric oxide and atomic oxygen. Because of these interconversions, nitric oxide and nitrogen dioxide are seldom found in isolation of each other in the occupational and ambient environments.

The major sources of high pollutant levels of NO_x in the atmosphere are the gasoline burning internal combustion engine and stationary industrial combustion facilities. A variety of sources found in occupational situations can result in exposure to localized concentrations of oxides of nitrogen. In general these will be associated with high temperature operations or a chemical process in which nitric acid, nitrates, or nitrites are involved. In the case of smokers, inhalation of tobacco smoke imposes a significant intermittent superimposition on the ambient and occupational levels of NO_x to which such individuals are circumstantially subjected. The overall exposure to NO_x varies considerably according to the geographical, meteorological, industrial and socioeconomic conditions of areas and communities, and to personal habits as well as occupational situation.

Nitric oxide and nitrogen dioxide are extremely aggressive substances and react immediately upon contact with the surface of the respiratory tract. Data are still lacking to describe with accuracy injurious effects directly attributable to low levels of nitric oxide. In contrast, nitrogen dioxide is clearly toxic; observations of its adverse effects on biological systems are numerous and well documented. Because of the intimate interdependence of these two nitrogen oxides, however, it is appropriate to look at the possible adverse effects of nitric oxide when considering air quality standards for nitrogen dioxide.

The NO_x that is free to diffuse from its source into the atmosphere is diluted, in general, to levels that cause little noticeable distress to the general population. It is important in the case of these oxides not to overlook the fact that, through atmospheric interactions, new reaction products can be formed, which, individually and/or in combinations may be

more toxic than the initial pollutant. The products associated with photochemical or "Los Angeles" smog have been widely studied; less is known about health effects of non-photochemical products such as nitric and nitrous acids and particulate nitrates. In certain occupational environments, actual NO_x levels can become appreciable in the absence of adequate control facilities.

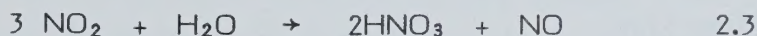
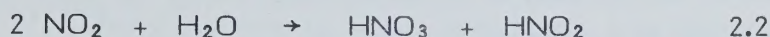
II. PROPERTIES AND REACTIONS OF NITRIC OXIDE AND NITROGEN DIOXIDE

1. General

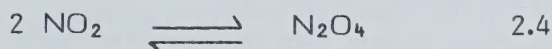
Nitric oxide is a colourless, odourless gas; its solubility in water is 2.37 cm³ per 100 cm³ at 60°C and 7.34 cm³ per 100 cm³ at 0°C. It is formed when oxygen and nitrogen from the air combine at high temperatures according to the reaction:



It is therefore produced by thermal reactions in flames, explosions and electric discharges. The equilibrium is a function of the flame temperature, the partial pressure of each gas and the movement of the gases through the different temperature zones. Nitric oxide will persist with other flame products when rapid cooling occurs. Nitrogen dioxide is a reddish-brown or dark orange gas having a characteristic pungent odour. It reacts with water to form nitric acid and either nitrous acid or nitric oxide.

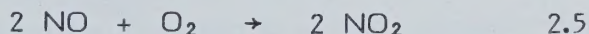


Both nitric oxide and nitrogen dioxide possess unpaired electrons and hence have free radical characteristics. They are extremely reactive; nitrogen dioxide is corrosive and strongly oxidizing. Both oxides may dimerize though this tendency is only slight in the case of nitric oxide. Nitrogen dioxide and its dimer, dinitrogen tetroxide exist in a strongly temperature dependent equilibrium:



Dinitrogen tetroxide is colourless and is obtained as a pure solid at temperatures below -9.3°C. The fraction of dimer present at atmospheric concentrations of nitrogen dioxide is negligible; in evaluating occupational exposure to the two forms, results are customarily expressed in terms of nitrogen dioxide. Both nitric oxide and nitrogen dioxide are formed when nitric acid reacts with reducing agents. With dilute acid, nitric oxide predominates while nitrogen dioxide is the major product formed from concentrated acid.

Nitrogen dioxide is formed by the atmospheric oxidation of nitric oxide.



The rate of this reaction decreases as the temperature increases. The rate of conversion is also highly dependent on the concentration of nitric oxide and is significant only when nitric oxide is present in high local concentrations. Once atmospheric dilution has reduced

the concentration of nitric oxide to a few ppm this reaction becomes extremely slow. Data on theoretical oxidation rates of nitric oxide in air at 20°C are presented in Table 1.

TABLE 1

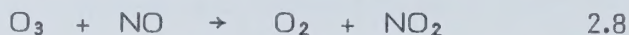
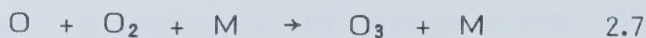
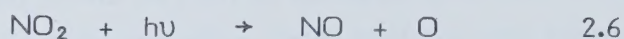
OXIDATION RATE OF NO IN AIR (20% O₂) at 20°C.

NO Concentration ppm	Oxidation Time		
	25%	50%	90%
10,000	8.4 sec	24 sec	3.6 min
1,000	1.4 min	4 min	36 min
100	14 min	40 min	6 hours
10	2.3 hours	7 hours	63 hours
1	24 hours	72 hours	648 hours

The presence of factors such as moisture, metal fumes, or ultraviolet radiation may influence the actual rate of conversion of nitric oxide to nitrogen dioxide.

2. Photochemical Reactions

In polluted atmospheres (i.e., those containing reactive hydrocarbons in the presence of NO_x) reactions other than the one described above are able to effect the conversion of nitric oxide to nitrogen dioxide, with the concurrent formation of secondary pollutants associated with "photochemical", or "Los Angeles Type", smog. Nitrogen dioxide, which initiates the process, is an efficient absorber of ultraviolet and visible radiation. At wavelengths between 290 and 420 nm the absorbed energy is sufficient to cause dissociation of nitrogen dioxide to nitric oxide and atomic oxygen, (reaction 2.6), the rate of nitrogen dioxide dissociation being directly proportional to the intensity of the light within the above wavelength range.



Atomic oxygen reacts with atmospheric oxygen producing ozone; collision of the ozone with another species, M, (normally molecular oxygen or nitrogen), allows transfer of excess energy thus preventing decomposition of the newly formed ozone, (reaction 2.7). In the absence of other reagents, ozone and nitric oxide would react to regenerate nitrogen dioxide and oxygen; (reaction 2.8). However, reactive hydrocarbons, especially olefins and certain

aromatics, react with oxygen atoms forming oxidized compounds and free radicals which in turn react with nitric oxide to produce more nitrogen dioxide. Other free radical reactions involving transient species such as hydroxyl and hydroperoxyl radicals and reactive pollutants such as carbon monoxide and aldehydes participate in a complex sequence of reactions in which the net result is the oxidation of nitric oxide to nitrogen dioxide and the accumulation of ozone. In addition to ozone and nitrogen dioxide, species such as peroxyacyl nitrates (PAN's) and other photochemical oxidants are produced. The components of photochemical smog have not been fully characterized, but it is suspected that they could pose additional and perhaps more serious hazards to humans than the primary pollutants.

In the absence of sunlight or a strong ultraviolet source, such reactions are not possible. This would be the case in a number of occupational environments; for example, underground parking facilities, mining and tunneling operations. Interactions of NO_x with other pollutants in such circumstances have probably not been widely investigated. Conversion of nitric oxide to nitrogen dioxide would almost certainly proceed by the slower thermal mechanism. In order to monitor effectively exposure to oxides of nitrogen, it is therefore desirable to conduct determinations for both nitric oxide and nitrogen dioxide. Other reactions occurring in mixtures of nitrogen dioxide, nitric oxide and water vapour ultimately lead to the formation of nitrous acid, nitric acid and nitrates.

3. Formation of N-nitrosamines

In the presence of secondary amines oxides of nitrogen can lead to the formation of secondary nitrosamines. These have been demonstrated to be carcinogenic in a number of animal studies. The reaction between secondary amines and nitrogen oxides is catalyzed under acidic conditions; nitrosamine formation may also occur in neutral media. Although the in vivo formation of nitrosamines has been demonstrated under a number of controlled conditions their production, following inhalation of nitrogen dioxide, has not been shown conclusively.

In the occupational environment the airborne formation of nitrosamines must also be considered. Low levels have been detected in the air of plants manufacturing primary and secondary amines. Although nitrogen dioxide was also present, current information is inadequate to establish with certainty the exact conditions under which airborne nitrosamines are formed in the workplace.

III. SOURCES AND LEVELS OF EXPOSURE

1. General Exposure

The major portion of global NO_x is produced by the bacterial transformation of nitrite and other biological processes. Man-made NO_x , however, is emitted in relatively small densely populated areas leading to high concentrations of nitrogen oxides in the direct vicinity of man. The levels of NO_x in urban atmospheres may be higher than those found in rural regions by as much as 10 to 100 times. Actual ambient concentrations in urban environments depend on the nature and the number of sources and will vary considerably with time, climatic conditions and distance from the source(s). Monthly averages from 10 to 100 ppb have been recorded in Canada; however peak levels, (1 hour maximum concentrations) approaching 600 ppb have been reported for Windsor and Ottawa.

The burning of oil, coal, natural gas and motor vehicle fuel accounts for well over 90% of technologically associated NO_x in the atmosphere. Relatively small quantities of NO_x arise from industries that manufacture or use nitric acid. Nitric oxide and nitrogen dioxide are also emitted on a nationwide basis from a number of smaller operations such as electroplating, engineering, welding, metal cleaning and detonation of explosives. Though making a negligible contribution to the total NO_x production, it is these sources that can result in high exposure levels in the occupational environment.

2. Occupational Exposure

The following groups of workers are most likely to be exposed to oxides of nitrogen:

Aniline makers	Explosives workers
Arc welders	Galvanizers
Blasters	Metal cleaners
Bleachers	Miners
Chemical workers	Picklers (metals)
Damascening workers	Torch cutters (metals)
Dye makers	Tunnellers
Electroplaters	Welders
Etchers	Metal refiners
Silo-fillers	Motion picture operators
Parking attendants	Glass blowers
	Garage mechanics

In addition any workers located in the vicinity of operations or processes having conditions conducive to the formation of NO_x e.g., furnaces, boilers, internal combustion engines, may undergo exposure.

Although a number of cases of adverse effects of occupational exposure to nitrogen oxides have been described in the literature, correlation, specifically with nitric oxide or nitrogen dioxide, is often complicated by the absence of data defining precisely the pollutant composition. In some studies nitric oxide and nitrogen dioxide levels were not reported separately; others failed to take into consideration the presence of other contaminants. Valid intercomparisons of various studies are also precluded because of non-standardized reporting procedures.

The relative proportions of nitric oxide and nitrogen dioxide produced by a number of work operations are summarized in Table 2. In general, it can be seen that high temperature operations favour the initial formation of nitric oxide; the ratio will change as atmospheric oxidation of nitric oxide to nitrogen dioxide occurs. Nitric acid dipping results in the immediate formation of excess nitrogen dioxide.

TABLE 2
APPROXIMATE DISTRIBUTION OF NITROGEN OXIDES GENERATED FROM
VARIOUS OPERATIONS

Source	% NO ₂	% NO
Carbon Arc	9	91
Oxyacetylene Torch	8	92
Cellulose Nitrate Combustion	19	81
Diesel Exhaust	35	65
Dynamite Blast	52	48
Acid Dipping	78	22

2.a. Welding and Cutting Operations

Data collected from field or controlled studies on nitric oxide levels resulting from arc or flame welding have generally been reported in terms of "nitrous gases", "nitrogen oxides" and even "nitrogen dioxide". However, in one group of experiments simulating cutting torch operations, it was shown that, 15 minutes after commencement of cutting, the nitrogen dioxide comprised 13% of total oxides. This increased to 33% after an additional 25 minutes; the rate of conversion of nitric oxide to nitrogen dioxide being consistent with the theoretical rate. In welding, the presence of ultraviolet light, ozone and other contaminants could lead to other reactions, including photochemical transformations of the type discussed in section 2, and hence large deviations from theoretical rates of conversion. One relevant study

demonstrated that approximately equal concentrations of nitric oxide and nitrogen dioxide totalling about 30 ppm remained essentially unchanged after two to three hours. However it must be remembered that, in the absence of an ultraviolet source, thermal oxidation at these levels would be extremely slow.

Levels of nitrogen oxides may be considerably reduced in the presence of hot metals owing to the decomposition of nitric oxide to nitrogen. Thus, maintaining flame contact with the metal should reduce worker exposure. Experiments have demonstrated that levels of nitrogen oxides may be reduced by factors ranging from 3 to as much as 7 times.

In general, exposure levels to nitrogen oxides resulting from welding and cutting operations can be extremely high ranging from a few ppm to several hundred ppm and will depend on a number of factors including, the nature of the operation, operating conditions, proximity of the source and the presence of other contaminants.

2.b. Motor Vehicle Exhausts

Exposure levels experienced by operators of ice resurfacing machines were shown to be as high as 40 ppm (reported in terms of nitrogen dioxide). Similar levels could presumably be experienced by personnel employed in facilities such as repair garages, underground parking areas and tunnel booths where ventilation is inadequate. Exposure would be mainly to nitric oxide since conversion of nitric oxide to nitrogen dioxide is relatively slow in the absence of sunlight. Adverse reactions occurring in occupational situations such as these cannot be attributed solely to NO_x owing to the co-existence of other harmful contaminants associated with motor vehicle exhausts.

2.c. Diesel Locomotive Exhausts

In 1960 Katz and Rennie reported an extensive study concerning exposure to diesel locomotive exhaust gases accumulating in the Canadian National Railway's St. Clair Tunnel. The tunnel which is 6032 feet in length links Sarnia, Ontario with Port Huron, Michigan. At the time of the study (1957) there was a lack of forced ventilation; this, together with the mode of operation of traffic using the tunnel, was anticipated to result in contaminant concentrations ranging greatly both as a function of time and location in the tunnel. During the three day testing period 104 trains passed through the tunnel; more than 2000 observations were made in order to determine the fluctuations and range of contaminant levels occurring under a variety of traffic conditions. Measurements were made separately for nitrogen dioxide and total nitrogen oxides; data for formaldehyde, sulphur dioxide, oxygen, smoke, particulate matter, carbon monoxide and carbon dioxide were also reported. For the total nitrogen oxides and nitrogen dioxide both instantaneous, or "snap", samples and average ten minute samples were collected.

Nitrogen dioxide levels were determined in 204 snap samples collected at predetermined intervals during and after the passage of 24 of the diesel trains. Mean values varied between 0.4 and 2.8 ppm with maximum concentrations ranging from 0.6 ppm to 15 ppm. The levels for the 10-minute time average samples ranged from 0.1 to 0.4 ppm. In the case of 177 snap samples collected during the passage of these test trains, the mean values for total nitrogen oxides (reported as nitrogen dioxide) varied from 9.1 to 38.4 ppm; the peak instantaneous concentration reached a level of 67 ppm.

The mean concentrations of nitrogen oxides and nitrogen dioxide found in the tunnel atmosphere over 24-hour test periods are shown in Table 3.

TABLE 3
MEAN CONCENTRATIONS OF NITROGEN DIOXIDE AND NITROGEN OXIDES
FOR SAMPLES COLLECTED DURING 24-HOUR PERIODS

			October 18, 1957			October 22, 1957			October 23, 1957		
Contaminant	Type of Sample	Station Number	5	6	7	5	6	7	5	6	7
Nitrogen Dioxide	Instantaneous	No. of Samples	24	22	20	24	40	22	18	17	17
		p.p.m.	1.0	0.5	1.3	1.0	2.5	2.1	1.6	0.6	1.9
	10-minute Average	No. of Samples	3	4	3	5	5	5	12	9	10
		p.p.m.	0.2	0.1	0.3	0.2	0.2	0.2	0.3	0.1	0.4
Total Oxides of Nitrogen (Calculated as NO ₂)	Instantaneous	No. of Samples	22	21	22	18	37	16	17	14	10
		p.p.m.	21.7	22.3	21.3	17.8	26.1	24.5	32.7	23.2	24.6

These data illustrate that the nitric oxide produced under the high combustion temperatures of diesel engines is oxidized relatively slowly to nitrogen dioxide in tunnel atmospheres. At the concentrations shown, efficient tunnel ventilation could remove the contaminants before appreciable conversion of nitric oxide to the more toxic nitrogen dioxide takes place.

2.d. *Explosives*

Underground blasting operations with both nitro explosives and gunpowder produce levels of nitrogen oxides up to 88 ppm; incomplete detonation, "misfires", can result in levels being higher by a factor of nearly two. Conventional powder shots may cause momentary concentrations of NO_x up to 56 ppm and 150 ppm after single and multiple firings respectively.

2.e. *Agricultural Silos*

Concentrations of nitric oxide and nitrogen dioxide may reach several hundred ppm during the decomposition process in a freshly filled agricultural silo. At these concentrations the distinctive brown colour of nitrogen dioxide may be discernible.

3. Tabacco Smoke

Intense exposure to nitrogen oxides occurs through inhalation of tabacco smoke. The NO_x content of cigarette, cigar and pipe smoke has been reported to range from 170 to as high as 1000 ppm. A significant proportion of this may be in the form of the more aggressive nitrogen dioxide. Non-smokers can also be affected by "indirect smoking".

4. Exposure to N-nitrosamines

Trace levels of secondary nitrosamines have been reported, both in workplace air, and in the air of urban communities, near chemical manufacturing plants. Concentrations reported for dimethylnitrosamine, for example, have ranged from 0.001 to nearly 1 ppb. However, the few studies so far reported have failed to rule out either the possible formation of these compounds during sampling, or their introduction into the environment due to the direct leakage of nitroso intermediates. Further studies are required to establish clearly the role of nitrogen dioxide in the formation of nitrosamines in the workplace environment.

IV. ANALYTICAL METHODS

A number of analytical procedures have been proposed for measuring NO_x concentrations in the air. Intercomparisons of data collected during different studies have been extremely difficult however, because of the absence of a reliable standardized procedure. Many of the methods used have involved oxidation of nitric oxide to nitrogen dioxide and hence estimation of the "total oxides" as nitrogen dioxide; this is particularly true in the case of published work on occupational exposures to nitrogen oxides. In order to determine each gas separately two basic approaches may be employed:

- i) Separation and determination of the nitrogen dioxide portion of a sample, followed by oxidation of the nitric oxide to nitrogen dioxide and determination by the same procedure;
- ii) Simultaneous collection of two samples, one of which is analyzed for nitrogen dioxide, the other for total nitrogen oxides; the nitric oxide contribution is then calculated by difference.

The analytical methods predominantly in use at the present time are:

- i) the colorimetric method by Saltzman,
- ii) coulometric determination;
- iii) chemiluminescence procedure.

The Saltzman method is based on the reaction of nitrogen dioxide with sulphanilic acid to form a diazonium salt that couples with N-(1-naphthyl)-ethylene-diamine dihydrochloride to produce a deeply coloured azo dye. This method has been used widely for both urban air pollution and occupational studies. It can be adapted for use as a manual procedure or in conjunction with automatic continuous recording equipment. Length-of-stain detector tubes using Saltzman reagent have also been developed; their use for occupational monitoring is described in Appendix II.

Coulometric instruments are based on the reduction of nitrogen dioxide by bromide or iodide. Bromine or iodine are released and produce a current which is measured with a microammeter; alternatively, voltage drop may be measured. Small, compact and relatively inexpensive devices suitable for continuous monitoring of nitrogen oxides have been designed.

The chemiluminescence analyser utilizes the principle of the photometric detection of chemiluminescence resulting from the gas phase reaction between ozone and nitric oxide. It is thus specific for nitric oxide. Nitrogen dioxide may be determined by difference. The

air sample is divided into two paths, one flowing directly to the reaction chamber, the other doing so after catalytic reduction of the nitrogen dioxide component to nitric oxide. Nitrogen dioxide may also be determined by a chemiluminescent reaction between oxygen atoms and nitrogen dioxide or by other indirect methods. Equipment costs for these methods are very high and often require experienced personnel for operation and maintenance. They could however become useful for continuous automatic monitoring of occupational areas.

Other procedures which have been used for nitrogen oxides measurement include gas chromatography employing electron-capture detection, and long path infra-red spectroscopy. The methods are not particularly suitable for application in the work environment.

In its recent report, the United States' National Institute for Occupational Safety and Health proposed methods for sampling and determining nitric oxide and nitrogen dioxide at concentrations normally encountered in the work environment. These are attached as Appendix I. The sampling method is recommended because of its simplicity, suitability for personal sampling and because samples remain stable during their shipment to the laboratory. The nitrogen dioxide sample is collected on a triethanolamine-impregnated molecular sieve surface. An identical sieve collects the nitric oxide portion after its conversion to nitrogen dioxide by a proprietary solid oxidizing material. The collected samples are subsequently analysed by the colourimetric procedure also described in Appendix I.

V. HEALTH EFFECTS

1. Nitrogen Dioxide

1.a. *Animal Studies*

Acute Effects - Depending on the duration of exposure, nitrogen dioxide levels ranging from 100 to 150 ppm are lethal to most animals; the LC₅₀ (15 min) for rats is about 400 ppm, pulmonary edema being the major cause of death. Generally the major toxic effect in animals is pulmonary inflammatory cellular reaction, with various degrees of edema causing injury to tissue.

Chronic and Subchronic Effects - Rats and hamsters, exposed to nitrogen dioxide concentrations over the range 12.5 ppm - 100 ppm, had hypertrophy and hyperplasia of bronchia, bronchiolar epithelium and alveoli. The time for appearance (from 4 to 10 weeks) and the intensity of the toxic effects were dose-related; these effects regressed following withdrawal from exposure. Rats exposed to nitrogen dioxide at a level of 100 ppm died within 24 hours. In another study, methemoglobin was noted in rat blood following exposure to 100 ppm. At 24 ppm, nitrate and nitrite ions were detected in the urine of rabbits. Monkeys, at 35-50 ppm (2 hr. exposure) showed a marked increase in respiratory rate with marked decrease in tidal volume.

Mice, rats, rabbits and dogs, exposed to nitrogen dioxide concentrations of 5-50 ppm for periods varying from 4 hours to 191 days showed dose-related macro- and microscopic pulmonary changes, emphysema, minor lung lesions, pulmonary edema (increased lung weight), and a large increase in the number of macrophages. At 2-25 ppm, polycythemia was noted in rats and monkeys. Squirrel monkeys and mice exposed to 5 ppm for 2 months showed increased susceptibility to infection by K. pneumonia and influenza virus. Monkeys exposed to 10-15 ppm showed a decrease in tidal volume but no change in respiratory rate; septal breaks and alveolar expansion were observed.

Rats, dogs, rabbits and mice, exposed to nitrogen dioxide concentrations of 2-5 ppm for periods equal to and greater than 18 months, exhibited a reduction of bronchiolar cilia, inhibition of normal exfoliation and appearance of cytoplasmic crystalloid inclusions; increase of lung weight however was insignificantly low. All animals exhibited decreased bactericidal activity.

Rats, guinea pigs and mice exposed to levels of 0.5 - 1.0 ppm for periods up to 40 weeks showed evidence of chronic respiratory diseases such as bronchitis and bronchopneumonia

indicating decreased bactericidal activity. There were minor macro- and microscopic changes in the lung which regressed following withdrawal from exposure.

Mice exposed continuously to 0.5 ppm nitrogen dioxide for periods from 3 to 12 months had minimal alveolar septal breaks and there was evidence of bronchiolar epithelial erosion. These disturbances, however, were not distinctly dose-related and interpretation in terms of nitrogen dioxide exposure is difficult.

The respiratory tract of animals under chronic or subchronic exposure conditions appears to be somewhat resistant to low concentrations of nitrogen dioxide, since no abnormalities were noticeable in the pulmonary function tests involving guinea pigs, rabbits, mice and beagles. These were exposed to concentrations ranging from 0.5 up to 5 ppm. It should be noted however that, under conditions of acute exposures, changes in the respiratory rates and tidal volumes were observed; these were completely reversible in animals that survived.

The oxygen partial pressure (P_{O_2}) in the brain tissue of rats was used as an indicator of lung function impairment by Zorn in 1975; an exposure of 6-8 hours at nitrogen dioxide concentrations of 0.5 - 20 ppm resulted in a dose-related decrease of P_{O_2} at all nitrogen dioxide levels.

Carcinogenesis, Mutagenesis and Reproduction - In 1965, it was suggested that nitrogen dioxide might be a tumour-promoting agent (accelerating the rate of appearance of lung adenomas). Mice were exposed to nitrogen dioxide levels of 5 ppm, 6 hr/day, 5 days/week for up to 16 months. Results were inconclusive due to the small sample size and to conflicting results of tumour incidence at different months after exposure. Further studies, with larger numbers of animals are needed before any definite conclusion can be drawn.

In another study (only a brief note) mice were intermittently exposed to nitrogen dioxide at 40 ppm for a period of ca. 18 months with no evidence of malignant lung tumours. The authors added that there was not an increasing incidence of lung cancer in workers exposed to nitrogen dioxide but gave no data in support of any of their statements. In a different study these authors exposed hamsters to a mixture nitrogen dioxide (40 ppm) and nitric oxide (20 ppm) for 16 months. Results revealed no carcinogenic action in the lung or in other organs. They reported the presence of adenomatous changes but results on control animals were absent to allow a comparison with controls.

In another study, the combined effects of nitrogen dioxide and benzpyrene were investigated in rats. Preliminary results indicated the presence of squamous cell carcinoma in the lung of one animal out of 30 exposed to 25 ppm of nitrogen dioxide with repeated 1 hour exposure to combined nitrogen dioxide and benzpyrene. Similar qualitative changes

in the lung tissue were observed in rats exposed to sulphur dioxide together with benzpyrene. However, the evidence of the carcinogenicity of nitrogen dioxide is questionable due to lack of complete results on a systematic study.

Evidence of mutagenesis by nitrogen dioxide in animal species has not been found in the literature. However, nitrous acid, a reaction product of nitrogen dioxide with water has been shown to have a potent mutagenic effect on the tobacco mosaic virus and E. coli.

In 1971, significant changes were reported in estrus, litter size, and fetal weights for rats exposed to nitrogen dioxide at 1.3 ppm for 12 hr/day over a 3-month period. No effects were noted at 0.07 ppm. Further research, however, is needed to define the limits of exposure at which these changes occur.

1.b. Human Studies

In 1967, experimental exposures to nitrogen dioxide at 4-5 ppm for 10-15 minutes were reported for five healthy adult men. Decrease in effective lung compliance was noted with corresponding increase in expiratory and inspiratory maximum viscous response.

In 1971, the effects of low concentrations of nitrogen dioxide on the respiratory gas exchange and airway resistance were reported in 88 chronic bronchitis patients (aged 37-72) who breathed 0.5 - 5.0 ppm nitrogen dioxide in air for 15 minutes. Between 1.5 and 5.0 ppm, a significant increase in airway resistance was noted. There was also a significant decrease in arterial oxygen partial pressure, and an increase in end-expiratory arterial pressure at 4-5 ppm.

In 1973, carbon monoxide diffusing capacity was measured in 16 healthy male volunteers who breathed 0.5-5.0 ppm of nitrogen dioxide in air for 15 minutes. A significant reduction in carbon monoxide diffusing capacity was noted at 5 ppm. No effects were noted below 1.5 ppm.

2. Nitrogen Dioxide in the Presence of Other Contaminants

2.a. Animal Studies

Tobacco Smoke - Exposure for 2 hours to 15 ppm nitrogen dioxide or 1 hour to 3% v/v tobacco smoke had only a slight effect (histopathologically) on the surface structure of hamster lungs. Sequential exposure (nitrogen dioxide followed by tobacco smoke) produced clearly identifiable alterations in the surface morphology; a marked loss of cilia was noted two days after exposure. This effect was not readily reversible during the observation period (no mention of pulmonary function tests). Seven days after exposure, the surface structure of the main bronchi and secondary airways was further disrupted; deep holes appeared among small patches of cilia in the mucosa. It was concluded that nitrogen dioxide and tobacco smoke acted synergistically.

Carbon - On exposure of guinea pigs to carbon particles and nitrogen dioxide, results depended on the sequence of exposure. Inhalation of carbon followed by nitrogen dioxide resulted in destructive microscopic changes within the lung, whereas inhalation of nitrogen dioxide followed by carbon did not cause the above changes. No mention of atmospheric levels and of the physiological response of the lung was made.

K. pneumoniae - Extensive short- and long-term studies were carried out on mice, rats, hamsters, rabbits and monkeys by a variety of authors to investigate the combined effect of nitrogen dioxide and K. pneumoniae at various levels (as high as 50 ppm and as low as 0.5 ppm of nitrogen dioxide). Results were indicative of a strong increase in susceptibility to infection at levels above 2.5 ppm of nitrogen dioxide, and of only a small increase in susceptibility at and below 2.5 ppm; the increase, however, was questionable at and below 1.0 ppm because of the fact that the control animals also had moderate pneumonitis.

Influenzal Virus - Exposure of mice vaccinated with influenzal virus to nitrogen dioxide caused a significant increase in mortality; the effect was related to the level of nitrogen dioxide in air.

Nitrogen dioxide is injurious to both the lining cells and phagocytic cells of the lung. It interferes with the efficiency of clearing of inhaled particles, including bacteria and viruses, from the airways and with the phagocytosis and digestion of such particles, mainly by macrophages, in the alveoli. Injury to the ciliary transport system is a significant toxic effect of nitrogen dioxide. This was characterized by (1) increased mortality rates, (2) reduced survival times and (3) reduced ability to clear inhaled infectious agents, as determined by the number of viable organisms cultured from the lungs.

Sulphur Dioxide - Rats and mice were exposed, for up to 5 months, to combinations of 3 ppm of nitrogen dioxide with 5-6 ppm of sulphur dioxide; only additive (and not synergistic) effects of the components were evident, as there was a significant decrease in the bacterial clearance.

Ozone - No synergistic effects occurred when nitrogen dioxide was examined in combination with ozone. Resistance to infection showed only an additive effect in mice at concentrations of 1.5 - 1.3 ppm nitrogen dioxide and 0.4 - 0.4 ppm ozone, the period of exposure being up to 17 hours.

2.b. Human Studies

Sulphur Dioxide - Exposure of humans to a mixture of 2.5 ppm nitrogen dioxide and 2.5 ppm sulphur dioxide produced a bimodal increase in both inspiratory and expiratory flow resistance. The first rise, which occurred immediately after exposure, corresponded to

the effect of sulphur dioxide alone. The second, maximal after 30 minutes after exposure, corresponded to the effect of nitrogen dioxide alone.

In another study, sequential exposure of nitrogen dioxide and later sulphur dioxide produced only a pseudoadditive effect on the pulmonary function tests (increase in airway resistance).

A well-organized and well-conducted study on the combined effects of nitrogen dioxide and sulphur dioxide is not available in the literature.

3. Nitric Oxide

3.a. *Animal Studies*

Acute Effects - Mice exposed to high concentrations of nitric oxide (2500 ppm) were narcotized in 6 to 7 minutes and died within 12 minutes. If, however, after 7 minutes the exposure was interrupted and the animals returned to fresh air, recovery was rapid and prolonged effects were not apparent. The survival of mice exposed to nitric oxide concentrations below 1000 ppm depended on the duration of exposure; at 310 ppm all mice survived an 8-hour exposure. Guinea pigs showed no change in pulmonary function after a four-hour exposure to nitric oxide levels ranging from 16 to 50 ppm.

At levels of 1000-5000 ppm cyanosis and methemoglobin formation was observed in animals that died; pulmonary edema was also noted.

An elevation of methemoglobin levels was detectable in the blood of rats exposed to nitric oxide concentrations ranging from 5 to 10 ppm (duration of exposure not specified). The increase was only slight and was completely reversible following withdrawal from exposure.

Chronic Effects - No data are available at present to describe the long-term toxic effects arising from low level exposure to nitric oxide.

3.b. *Human Studies*

In experiments conducted using 191 healthy adults exposed for 15 minutes to nitric oxide concentrations up to 40 ppm the following observations were made:

- a) The diffusion capacity of the lung to carbon monoxide did not decrease at and below 30 ppm;
- b) an increase in airway resistance was not significant at and below 20 ppm;
- c) no significant changes in the arterial oxygen tension could be detected at and below 20 ppm;

- d) an increase in methemoglobin concentration was not significant at and below 20 ppm.

Over the concentration range 20-30 ppm, the changes in lung function abnormalities and methemoglobin concentration are only minimal and probably would not result in any noticeable discomfort to workers.

No data are available concerning the toxic effects of nitric oxide on persons with chronic bronchitis.

4. Epidemiology

In 1972, the prevalence of emphysema was reported in coal miners exposed sporadically to oxides of nitrogen (38-345 ppm expressed as nitrogen dioxide). Emphysema was found in 84 of the 100 miners studied. However, no satisfactory control group was studied and the results were further complicated by the association of coal worker pneumoconiosis with emphysema.

In 1970, conjunctivitis and pharyngitis were reported in five men welding zinc-plated steel in a confined space. Measurements showed total oxides of nitrogen, (expressed as nitrogen dioxide), to be in the 4-20 ppm range. The duration of exposure was not stated. The toxic effects subsided 18 hours after exposure.

In 1941, a slight increase (ca. 1.5% increase) in the levels of methemoglobin was found in the blood of four arc-welders exposed to oxides of nitrogen in the 2.0 - 10.3 ppm range (expressed as nitrogen dioxide). The duration of exposure was not given.

In 1972, complaints of sporadic cough, mucopurulent expectoration and dyspnea on exertion were reported in 70 men (aged 26-48) who worked in a chemical plant for 8 hours daily over a period of approximately 5 years and who were described as being exposed to only oxides of nitrogen. Concentrations between 0.4 to 2.7 ppm were reported (expressed as nitrogen dioxide). These workers exhibited no abnormalities according to chest X-ray; blood pH, etc. There was a slight but significant decrease in serum proteins, urinary amino acids and glycoproteins. However, correlation of the observed effects specifically with nitrogen dioxide are questionable due to inadequate characterization of the work environment, absence of spirometry changes, lack of evidence of a controlled diet in relation to urinary excretion of amino acids and glycoproteins, and omission of evidence on the relation between urinary excretions and emphysema.

In 1937, symptoms of chronic poisoning with oxides of nitrogen were reported in 127 printing shop and sulphuric acid plant workers (concentrations less than 2.8 ppm). The symptoms were dental erosion and gingivitis, emphysema, polycythemia and pulmonary tuberculosis, cardiovascular hypotonia and bradycardia. However, the presence of dental erosion suggests exposure to mists of sulphuric and nitric acids. Furthermore, due to lack of details on analytical methods, the relevance of this study is questionable.

5. Effects of N-nitroso Compounds

Isolated experimental (animal) studies indicate that inhalation of relatively high concentrations of secondary nitrosamines for short periods of time can result in liver damage, severe hematologic changes as well as carcinomas of the nasal cavity, trachea and lungs. The concentrations involved were approximately 10^6 times greater than those reported in the occupational environment. No animal data have been found on the chronic effects of long-term exposure at low airborne levels of nitrosamines, or on the in vivo formation of N-nitroso compounds from inhalation of the oxides of nitrogen. Furthermore, no epidemiological data exist indicating chronic effects in humans exposed to extremely low levels of airborne secondary nitrosamines. Therefore, the currently available data base is insufficient to comment on and establish the degree of risk from such low concentrations to occupationally exposed workers.

VI. BASIS FOR A RECOMMENDED STANDARD

1. Nitrogen Dioxide

Animal studies conducted under conditions directly comparable with those found in occupational situations, (i.e., long-term intermittent exposure for 8 hours per day, 5 days per week at low concentrations), were not found in the literature. Two studies approximating these conditions should be mentioned. Dogs exposed to 1 ppm of nitrogen dioxide, 6 hours per day, 5 days per week for a period of 1 year exhibited minimal macro- and microscopic changes of the pulmonary system, thickening of alveolar septa and chronic inflammatory cells. Guinea pigs exposed to nitrogen dioxide levels of 1 ppm over a period of 6 months, 8 hours per day, 5 days per week, also showed minor macro- and microscopic changes in the lung; there was also evidence of chronic respiratory disease such as bronchitis, bronchopneumonia and foci of emphysema. No abnormalities in the physiologic response of the lung were noted in either of these studies.

Under conditions of continuous exposure of 1 ppm of nitrogen dioxide in air, animals exhibited all the effects noted in the two studies above; the intensity, however, was somewhat greater. No abnormalities were noted in lung function tests.

In all the above studies the macro- and microscopic changes in the pulmonary system regressed completely following withdrawal from exposure to nitrogen dioxide.

Evidence of biological disturbances has been elicited by continuous exposure of mice to nitrogen dioxide levels as low as 0.5 ppm over periods of 3 to 12 months. These effects were not distinctly dose-related and could not be attributed specifically to nitrogen dioxide exposure.

Thus, a "no-effect level" was not clearly demonstrated in any of the available animal studies. However, since the morphological injury to the lung and evidence of chronic respiratory disease were minimal after exposure to 1 ppm of nitrogen dioxide, (under conditions approximating those found in occupational situations), this level can be taken as the "lowest effective level" or "threshold toxic level" for animals.

Extensive animal studies have strongly indicated an increased susceptibility to infection by K. pneumoniae and influenzal virus at moderate and high concentrations of nitrogen dioxide in air. At low concentrations (i.e., 1 ppm), this increased susceptibility was minimal and could not be identified definitely with exposure to nitrogen dioxide.

Epidemiological studies which clearly delineate a safe level for human exposure to nitrogen dioxide are not yet available. Existing epidemiological studies, for the most part, contain errors, omissions, inconsistencies and are therefore unreliable for establishing a safe exposure level. The results of human studies conducted under controlled conditions may be used (in conjunction with those from animal studies) to establish an occupational exposure limit for nitrogen dioxide.

A reduction in effective lung compliance with a corresponding increase in inspiratory and expiratory maximum viscous resistance was found for normal adult males exposed for 10-15 minutes to nitrogen dioxide at a concentration of 4-5 ppm. Significant decreases in arterial oxygen tension and single breath carbon monoxide diffusing capacity were also noted. No data are available for levels below 4-5 ppm and hence it is not known whether the 4-5 ppm level is the "threshold toxic level" for healthy people. A "no effect level" was demonstrable in chronic bronchitis patients at the 1.0 ppm level. Abnormalities were noted in lung functions in patients exposed at and above 1.5 ppm for 15 minutes; no effects were observed at levels 0.5 to 1.0 ppm. Thus the "threshold toxic level" was 1.5 ppm in chronic bronchitis patients. It must, however, be pointed out that, in view of the morphological injury to the lung shown in animal studies at the 1 ppm level, the "no effect level" in humans may only be a "no apparent-effect level", since physical lung injury can only be verified microscopically after death.

2. Nitric Oxide

As with nitrogen dioxide, animal studies conducted using nitric oxide have not reflected conditions typically found in the occupational environment. Long-term studies of continuous exposure are also not available. There is presently no evidence to suggest that long-term exposure to low levels of nitric oxide would have significant deleterious effects.

In the absence of sound data on which to base a standard for nitric oxide NIOSH has recommended that the United States' federal standard of 25 ppm be adopted as a time weighted average for up to 10 hours per day, 40 hours per week.

Based on pulmonary function observations, a "no effect level" of 50 ppm was noted in the acute animal studies. If the elevation of methemoglobin is considered as a toxic effect, then studies using rats would suggest a "no effect level" of 5 ppm. However, the latter parameter has not been shown to result in a significant toxic effect.

With reference to the human studies a "no effect level" of 20 ppm was indicated, based on lung function tests and observed methemoglobin concentrations. However, further experiments are needed to clearly define the dose-response relationship on lung function, and long-term morphological effects on the lung, before a recommendation to set a standard at or below this level can be made.

VII. RECOMMENDATIONS

1. Workers should not be exposed to nitrogen dioxide levels greater than a ceiling concentration of 1 ppm by volume (1.8 mg m^{-3}), as determined by a sampling time of 15 minutes.
2. In the absence of data clearly defining levels at which nitric oxide becomes deleterious to health it is recommended that exposure to this substance should not occur at a concentration greater than 25 ppm by volume (30 mg m^{-3}), determined as a time weighted average exposure for up to 10 hours per day and 40 hours per week.
3. Animal experiments have demonstrated a definite synergistic effect when exposure to nitrogen dioxide occurs in the presence of tobacco smoke. Workers should therefore be discouraged from smoking when the presence of nitrogen dioxide is suspected.

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APPENDIX I

PROPOSED ANALYTICAL METHODOLOGY FOR NITROGEN DIOXIDE AND NITRIC OXIDE

- A. Method for Sampling Nitrogen Dioxide and Nitric Oxide.
- B. Analytical Method for Nitrogen Dioxide and Nitric Oxide.
- C. Comments on the Proposed Analytical Procedures.

Note: Parts A and B of this appendix have been reproduced without change from the NIOSH report, Criteria for a Recommended Standard - Occupational Exposure to Oxides of Nitrogen (Nitrogen Dioxide and Nitric Oxide).

A. METHOD FOR SAMPLING NITROGEN DIOXIDE AND NITRIC OXIDE

The recommended method is adapted from procedures described by Blacker (211) and by Levaggi et al (212). This method is highly adaptable to personal monitoring, and it offers a number of advantages over available bubbler-type methods.

Principle

The following sampling method for nitrogen dioxide and nitric oxide in air employs collection of the NO₂ on a triethanolamine-impregnated molecular sieve surface, oxidation of the NO to NO₂ by a solid oxidizer, and collection of the converted NO on another section of triethanolamine-impregnated solid sorbent. The trapped NO/NO₂ is removed with an absorbing solution and the concentrations are determined by reading the color of the solution with a spectrophotometer.

General Requirements

Both nitrogen dioxide and nitric oxide concentrations shall be determined within the worker's breathing zone and shall meet the following criteria in order to evaluate conformance with the standard:

- (a) Samples collected shall be representative of the individual worker's exposure.
- (b) Sampling Data Sheets shall include:
 - 1. The date and time of sample collection.
 - 2. Sampling duration.
 - 3. Volumetric flow rate of sampling.
 - 4. A description of the sampling location
 - 5. Other pertinent information.

Breathing Zone Sampling

Breathing-zone samples shall be collected as near as practicable to the worker's face without interfering with his or her freedom of movement and shall characterize the exposure from each job or specific operation in each production area.

(a) Sampling Equipment

A calibrated personal sampling pump capable of operating at 50 cc/min, $\pm 5\%$, and a solid sorbent sampling tube containing 400 mg of triethanolamine (TEA-impregnated molecular sieve (type 13X, 30-40 mesh molecular sieve), a gap of 12 millimeters, 800 mg of #1900277

oxidation material from the Dragerwerk Company of Germany, and another 400 mg section of the TEA sorbent, all packed in a 5-mm ID, 7-mm OD glass tube. The ends of the tube are flame sealed (see Figure 1).

(b) Reagents

1. Purity - All chemicals should be analytical grade.
2. Nitrogen dioxide absorbent - Add 25 g of triethanolamine to a 250-ml beaker; add 4 g of glycerol, 50 ml of acetone, and sufficient distilled water to bring the volume up to 100 ml. To the mixture add about 50 cc of 30- to 40- mesh molecular sieve 13X (MCB No. MX 1583-1). Stir and let stand in the covered beaker for about 30 minutes. Decant the excess liquid and transfer the molecular sieve to a porcelain pan which is then placed under a heating lamp until most of the moisture has evaporated. Complete the drying in an oven at 110°C for 1 hour. Store in a closed glass container. (211)
3. Oxidizer - The oxidizer used in the sampling train is from Dragerwerk of The Federal Republic of Germany. Exact preparation of this oxidizer is proprietary, but the material is available from Dragerwerk through its US distributor, National Mine Safety Company. Substances of equivalent oxidizing characteristics may be used.

(c) Sampling Procedure

Immediately before sampling, the ends of the sampling tube are broken to provide an opening approximately one-half the internal diameter of the tube. The tube should be placed in a vertical position during sampling to avoid channeling. Air being sampled should not be passed through any hose or tubing before entering the sampling tube. Set the flow rate at 50 cc/min and record the starting time and initial counter reading (if applicable). The sampling tube is attached to the worker's clothing to sample from the worker's breathing zone. The sample is collected at 50 cc/min for a minimum 15-minute period. A minimum sample volume of 0.75 liter must be taken to measure 0.5 ppm NO₂. Sample volumes should not exceed 1.5 liter if nitric oxide concentrations of 50 ppm or greater are expected. When the sample has been taken, record the time and final counter reading.

The tubes should be sealed with appropriate plastic caps immediately after sampling. Masking tape is a suitable substitute for sealing the tubes. One sampling tube should be handled in the same manner as the sample tubes (break, seal, and transport), except for the taking of an air sample. This tube should be labeled as a blank. At least one blank tube should be provided for every 20 samples.

Shipping

After sampling, the tubes should be capped and labeled. The tubes should be packed with cushioning material to prevent the tubes from being broken in transit.

Calibration of Sampling Trains

Since the accuracy of an analysis can be no greater than the accuracy of the volume of air which is measured, the accurate calibration of a sampling pump is essential to the correct interpretation of the pump's indication. The frequency of calibration is dependent on the use, care, and handling to which the pump is subjected. In addition, pumps should be recalibrated if they have been misused or if they have just been repaired or received from a manufacturer. If the pump receives hard usage, more frequent calibration may be necessary.

Ordinarily, pumps should be calibrated in the laboratory both before they are used in the field and after they have been used to collect a large number of field samples. The accuracy of calibration is dependent on the type of instrument used as a reference. The choice of a calibration instrument will depend largely upon where the calibration is to be performed. For laboratory testing, primary standards such as a spirometer or soap bubble meter are recommended, although other standard calibrating instruments such as a wet test meter or dry gas meter can be used. The actual setup will be the same for all instruments. Instructions for calibration with the soap bubble meter follow. If another calibration device is selected, equivalent procedures should be used.

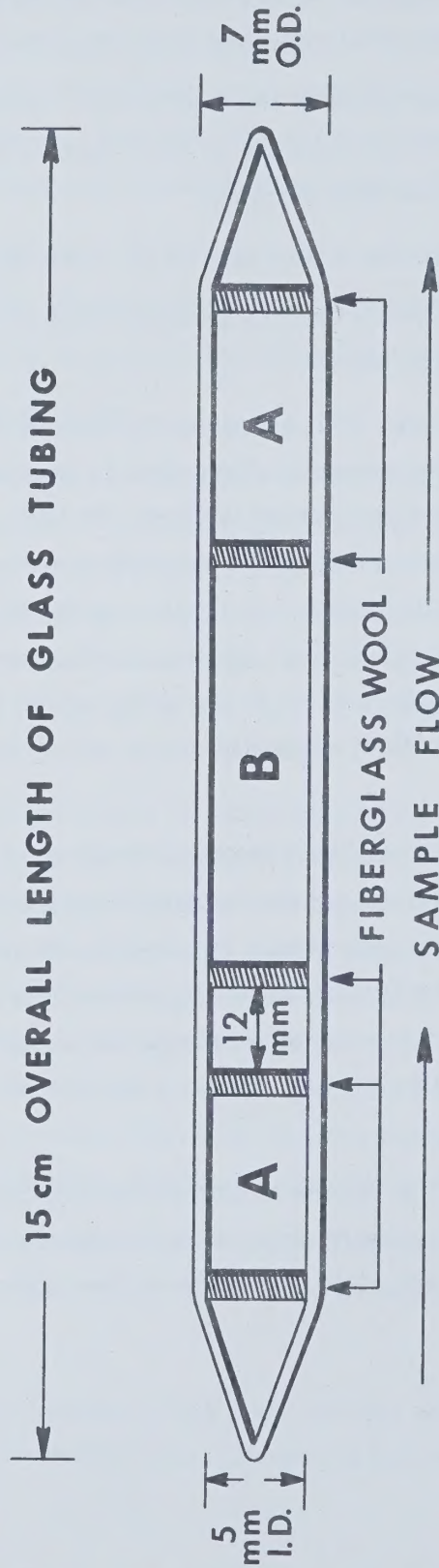
Flowmeter Calibration Test Method - For calibration of low flow pumps, i.e., 50-200 cc/min, a soap bubble meter with calibration marks from 1 to 100 ml is recommended.

1. Procedure

- (i) Check the voltage of the pump battery with a voltmeter to assure adequate voltage for calibration. Charge the battery if necessary.

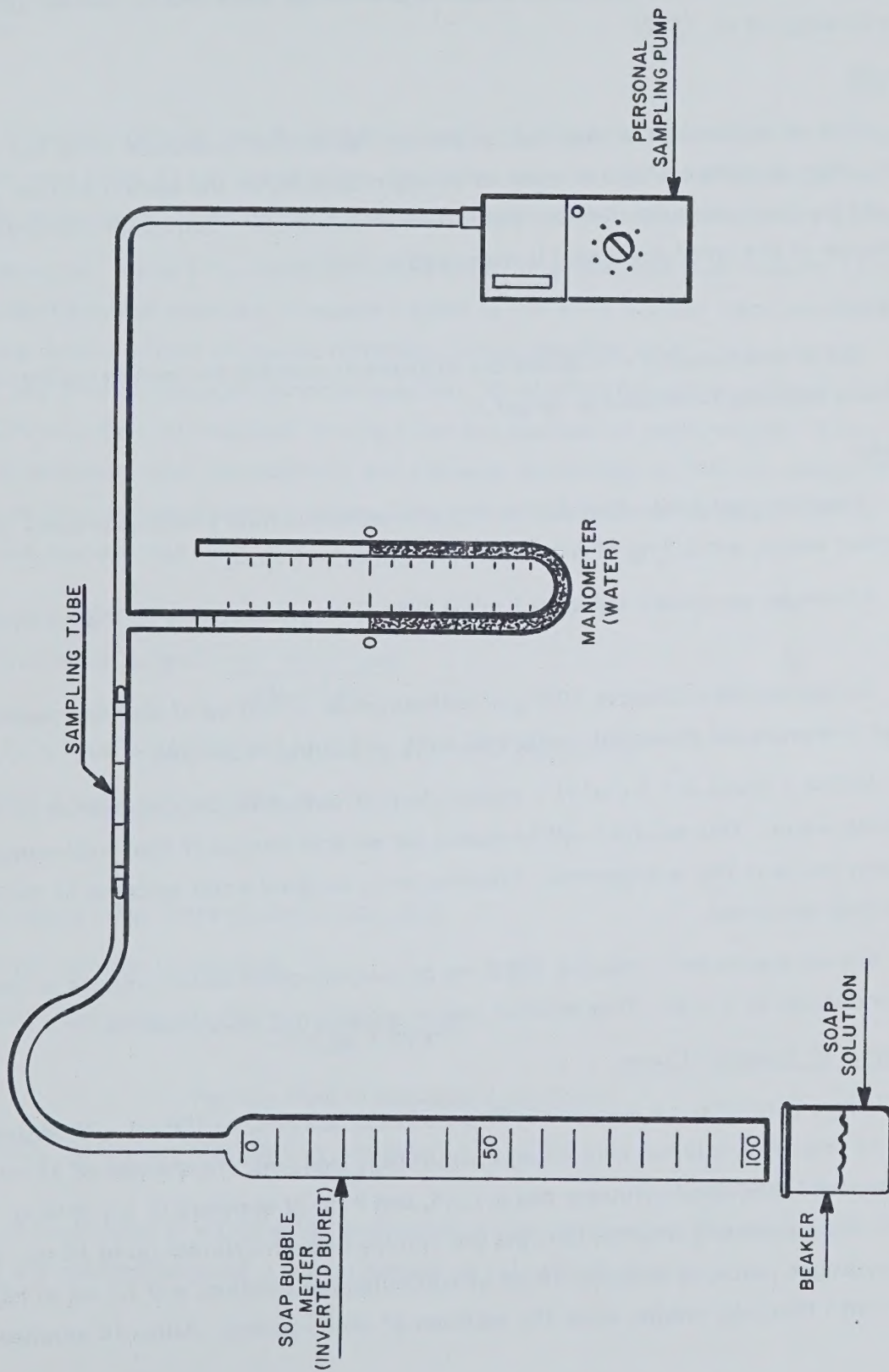
- (ii) Assemble the sampling train as shown in Figure 2, connecting the sampling tube in line between the soap bubble meter and the water manometer and then connecting the personal sampling pump after the manometer.
- (iii) Turn the pump on and moisten the inside of the soap bubble meter by immersing the buret in the soap solution and draw bubbles up the inside until they are able to travel the entire buret length without bursting.
- (iv) Adjust the pump rotameter to provide a flow rate of 50 cc/minute.
- (v) Check the water manometer to ensure that the pressure drop across the sampling train does not exceed 2.5 inches of water.
- (vi) Start a soap bubble up the buret and, with a stopwatch, measure the time it takes for the bubble to move from one calibration mark to another. For a 100-ml buret, a convenient calibration volume is 50 ml. At the same time, record the initial and final counter readings as the bubble travels between the chosen calibration marks on the bubblemeter. This can be accomplished by quickly reading the counter numbers when the soap bubble passes the calibration marks while the pump is running, or the pump can be turned off when the soap bubble reaches the final calibration mark and a counter reading taken.
- (vii) Repeat the procedure in (vi) above at least 2 times, average the results, and calculate the flow rate by dividing the volume between the preselected marks by the time required for the soap bubble to traverse the distance. Also calculate the pump stroke factor (cc/stroke) by subtracting the initial counter reading from the final counter reading, thus obtaining the number of strokes, and dividing this number into the volume over which the strokes were recorded.
- (viii) Data for the calibration include the volume measured, number of pump strokes measured, elapsed time, pressure drop, air temperature, atmospheric pressure, serial number of the pump, date, and name of the person performing the calibration.

FIGURE 1 - NITROGEN DIOXIDE/NITRIC OXIDE SAMPLING TUBE



- A. 400mg TRIETHANOLAMINE-IMPREGNATED TYPE 13X,
30-40 MESH MOLECULAR SIEVE**
- B. 800mg OF OXIDATION MATERIAL No.1900277 FROM DRAGER
COMPANY OF GERMAN, SUPPLIED BY NATIONAL MINE SERVICE CO.**

FIGURE 2 - CALIBRATION SCHEME FOR PERSONAL SAMPLING
PUMP AND SAMPLING TUBE



B. ANALYTICAL METHOD FOR NITROGEN DIOXIDE AND NITRIC OXIDE

The recommended method is based on procedures described by Blacker (211) and by Levaggi et al. (212)

Principle

The nitrogen dioxide absorbed on the first section of molecular sieve and the nitrogen dioxide, after oxidation of nitric oxide to nitrogen dioxide, on the second section of molecular sieve are treated with sulfanilamide and N-1-naphthylethylenediamine dihydrochloride. Absorbance of the color developed is measured at 540 nm.

Apparatus

Spectrophotometer - A laboratory instrument suitable for measuring the absorbance at 540 nm, utilizing 1-cm cells or larger.

Reagents

Absorbing solution - Dissolve 15.0 g of triethanolamine in approximately 500 ml of distilled water, add 0.5 ml of n-butanol, and dilute to 1 liter.

Hydrogen peroxide - Dilute 0.2 ml of 30% hydrogen peroxide to 150 ml with distilled water.

Sulfanilamide - Dissolve 10.0 g of sulfanilamide in 400 ml of distilled water. Add 25 ml of concentrated phosphoric acid, mix well, and dilute to 500 ml.

NEDA - Dissolve 0.5 g of N-1-naphthylethylenediamine dihydrochloride in 500 ml of distilled water. This solution will be stable for several months if kept well-stoppered in a brown bottle in the refrigerator. Alternatively, weighed small amounts of the solid reagent may be stored.

Standard solution - Dissolve 150.0 mg of reagent-grade sodium nitrite in distilled water, and dilute to 1 liter. This solution contains 100 μg of NO_2 (ion)/ml.

Preparation of Standard Curve

Dilute 2 ml of stock standard (100 μg of NO_2 (ion)/ml) to 100 ml with absorbing solution to prepare a solution containing 2 μg of NO_2 (ion)/ml. To a series of 25-ml glass-stoppered graduated cylinders add 0, 1, 3, 5, and 7 ml of standard (2 μg of NO_2 (ion)/ml). Add absorbing solution to bring the volume in each cylinder up to 10 ml. Add 1 ml of hydrogen peroxide solution, 10 ml of sulfanilamide solution, and 1.4 ml of NEDA solution, with thorough mixing after the addition of each reagent. Allow 10 minutes for

complete color development and measure absorption at 540 nm, using the treated blank to zero the spectrophotometer. Prepare the standard curve by plotting absorbance versus concentration.

Procedure

With a tweezer remove and discard the glass wool plug from one end of the nitrogen dioxide sample tube (Part A) and transfer the molecular sieve to a 25-ml glass-stoppered graduate. Add absorbing solution to make the volume up to 20 ml, and then shake vigorously for about 30 seconds. Allow a few minutes for the solids to settle, and then transfer 10 ml to a 25-ml glass-stoppered graduate. Prepare a blank in the same manner from unexposed molecular sieve obtained from an unused nitrogen dioxide absorber tube. To the sample and the blank add 1 ml of hydrogen peroxide solution, 10 ml of sulfanilamide solution, and 1.4 ml of NEDA solution with thorough mixing after the addition of each reagent. Allow 10 minutes for complete color development and measure absorbance at 540 nm, using the treated blank to zero the spectrophotometer. Determine NO₂ (ion) in the aliquot of the sample from the standard curve.

Calculations

$$\text{ppm (v/v) of NO}_2 \text{ (gas)} = \frac{\mu\text{l NO}_2 \text{ (gas)}}{\text{liters (air)}}$$

$$1 \mu\text{l NO}_2 \text{ (gas)} = 1.88 \mu\text{g NO}_2 \text{ (gas) at 25 C and 760 mmHg}$$

$$1 \mu\text{g NO}_2 \text{ (gas)} = 0.63 \mu\text{g NO}_2 \text{ (ion)}$$

If

r = sampling rate, liters of air/minute, and

t = sampling time in minutes,

$$\mu\text{l NO}_2 \text{ (gas)} = \frac{\mu\text{g NO}_2 \text{ (ion) in aliquot} \times 2}{1.88 \times 0.63}$$

$$= \text{mg NO}_2 \text{ (ion) in aliquot} \times 1.69, \text{ then}$$

$$\text{ppm NO}_2 \text{ (gas)} = \frac{\mu\text{g NO}_2 \text{ (ion) in aliquot} \times 1.69}{r \times t}$$

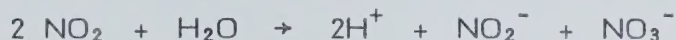
The concentration of nitric oxide, expressed in ppm of nitrogen dioxide (gas), is equivalent to the concentration of nitrogen dioxide as calculated above.

REFERENCES

211. Blacker J.H. Triethanolamine for collecting nitrogen dioxide in the TLV range. Am. Ind. Hyg. Assoc. J 34: 390-95, 1973.
212. Levaggi D.A., Siu W., Feildstein M. A new method for measuring average 24-hour nitrogen dioxide concentrations in the atmosphere. J. Air. Pollut. Control Assoc. 23: 30-33, 1973.

C. COMMENTS ON THE PROPOSED ANALYTICAL PROCEDURES

The reliability of photometric determinations of nitrogen dioxide based on the Saltzman procedure has been questioned owing to discrepancies regarding the conversion factor for nitrogen dioxide to the nitrite ion (NO_2^-). It is the nitrite ion which combines with reagents to form the azo dye. Theoretically 1 mole of nitrogen dioxide should react with water to produce 0.5 mole of nitrite ion.



In practice, however, this is not the case; at low ambient concentrations the conversion factor is close to unity, whereas, at the higher levels generally associated with occupational environments, it is nearer 0.75.

Conversion factors obtained using triethanolamine absorbers, (either as a liquid or held on a solid absorber), are again inconsistent. Over the range 3 to 10 ppm of nitrogen dioxide, factors varied from 0.56 to 0.76 (mean of 49 tests was 0.63). In another study, using nitrogen dioxide concentrations two orders of magnitude lower, conversion factors averaging 0.85 were found. Some caution may therefore be necessary in utilizing data obtained by this technique.

Another possible problem in the proposed methodology is the incomplete oxidation of nitric oxide to nitrogen dioxide. Under field conditions and in routine application, the oxidation efficiency using reagents such as permanganate or chromate has often been well below 100%. The solid oxidant recommended in the proposed sampling procedure is a proprietary formulation. No detailed information was given concerning the oxidation efficiency of this medium.

Tests conducted by NIOSH using the recommended sampling train indicated that "recovery rates for nitrogen dioxide were greater than 90% for samples generated at concentrations between 0.8 and 5.8 ppm. The average recoveries for nitric oxide were 97.4, 106, 84 and 67% for sample concentrations at 8.6, 11.0, 24.0 and 50.0 ppm, respectively. The total coefficient of variation was 7.2% for nitrogen dioxide and 5.5% for nitric oxide".

Inconsistencies may also be introduced by the lack of commercially available gas mixtures suitable for calibration purposes.

APPENDIX II

DETERMINATION OF EXPOSURE AREAS TO NITROGEN DIOXIDE WITH
DETECTOR TUBES AND WITH PORTABLE DIRECT-READING INSTRUMENTS

Note: This appendix has been reproduced without change from the NIOSH report, Criteria for a Recommended Standard - Occupational Exposure to Oxides of Nitrogen (Nitrogen Dioxide and Nitric Oxide).

DETERMINATION OF EXPOSURE AREAS TO NITROGEN DIOXIDE WITH DETECTOR TUBES AND WITH PORTABLE DIRECT-READING INSTRUMENTS

Detector Tubes

(a) Atmospheric Sampling

1. Equipment Used

A typical sampling train consists of a detector tube with a corresponding sampling pump. A specific manufacturer's pump may only be used with his detector tubes because these are normally integrated units.

2. Sampling Procedures

A specific procedure depends on the manufacturer's instructions but normally consists of breaking both tips off a detector tube, inserting the tube into the pump, and taking a specific number of strokes with the pump.

3. Handling and Shipping of Samples

Detector tubes are not stable with time because the stain in some tubes fades in a few minutes. The tubes should be read immediately in accordance with the manufacturer's instructions and charts and no attempt should be made to save the used tubes.

(b) General Principles

Gas detector tubes contain a chemically impregnated packing which indicates the concentration of a contaminant in the air by means of a chemically produced color change. The color changes are not permanent or stable, so the stained tubes must be read immediately after the samples are taken. The length of stain or color intensity is read according to the manufacturer's instructions and may involve comparing the stain with a chart, a color comparator, or a direct concentration reading from calibration marks on the tube. Detailed descriptions are provided by individual manufacturer's instructions.

Tubes obtained from commercial sources which bear the certified seal of NIOSH adhere to the requirements as specified for Certification of Gas Detector Tube Units in 42 CFR Part 84 (Federal Register 38:11458, May 8, 1973). A user may perform his own calibration on commercially

acquired tubes by generating accurately known concentrations of nitrogen dioxide in air and correlating concentration with stain length or color intensity.

The use of detector tubes with their respective pumps for compliance purposes is inappropriate because sampling times are necessarily very brief; thus, an excessive number of sampling periods would be required to permit calculation of a time-weighted average in the case of nitric oxide. In addition, the accuracy of detector tubes is limited (see (e) below).

(c) Range and Sensitivity

Certification standards require that certified tubes have a range of from 1/2 to 5 times the time-weighted average concentration for the duration of the sampling period. The sensitivity varies with tube brands.

(d) Interferences

Interferences vary with tube brands. The manufacturer's instructions must be consulted.

(e) Accuracy

Certification standards under the provisions of 42 CFR Part 84 (Federal Register 38:11458, May 8, 1973) specify reliability to within $\pm 25\%$ of the actual concentration in the range of 0.75 to 5 times the standard and $\pm 35\%$ in the range from 0.5 up to, but not including, 0.75 times the standard.

(f) Advantages and Disadvantages

The use of detector tubes is relatively inexpensive and rapid. There is far less time lag than that experienced with laboratory analytical procedures. Rapid detecting units are valuable for determining whether a hazardous condition exists at a given location at a given time so that workers may be evacuated or suitable protective devices provided. In addition, industrial operators and process engineers need inexpensive and rapidly responsive devices for day-to-day evaluation of the atmospheric levels in a work area.

In evaluating measurements performed with detector tubes, interferences, difficulty in endpoint readings, and possible calibration inaccuracies must all be considered. These factors

affect the accuracy of detector tubes. Thus, the use of such tubes must be limited to estimating the concentration of the contaminant.

Portable Direct-Reading Instruments

Several portable direct-reading instruments for the measurement of occupational exposures to nitrogen dioxide are available. With proper calibration and maintenance, they can be more sensitive and accurate than detector tubes, and they provide even more rapid indications of levels of exposure. Such instruments serve useful purposes by providing immediate on-the-spot information as to levels of nitrogen dioxide concentrations in work areas. This makes them particularly useful for evaluating the need for and effectiveness of control measures. In view of their size and weight, they are not practicable to use for personal sampling. Weights range from about 10 pounds to more than 25 pounds. The instruments do not give information on the levels of any nitric oxide present. Prices of commercially available nitrogen dioxide direct-reading meters are generally in the range of \$1,000 to \$2,000.

A NIOSH publication (228) has evaluated four commercially available direct reading nitrogen dioxide instruments. The publication discusses such factors and characteristics as portability, ease and simplicity of operation, completeness of instructions in the operation manual, maintenance procedures, direct reading capabilities, cost, ability to operate as a continuous monitor, cost and availability of replacement components, range of concentrations measured, accuracy of manufacturer's calibration, zero drift, response time, stability of calibration setting, ability to record continuously, linearity of response, specificity for nitrogen dioxide, severity of interferences, ease of calibration and zeroing, effects of temperature and humidity, durability, shipping problems, sensitivity, and life of components used to measure nitrogen dioxide.

REFERENCES

228. Johnson B.A. Evaluation of portable direct-reading NO₂ meters - NIOSH Technical Information, HEW Publication No. (NIOSH) 74-108. Cincinnati, US Dept. of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, Division of Laboratories and Criteria Development, 1974, 31 pp.
229. A Recommended Standard...An Identification System for Occupationally Hazardous Materials, HEW Publication No. (NIOSH) 75-126. US Dept. of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, 1974, 63 pp.

